
Klf2 and Tfcp2l1, Two Wnt/beta-Catenin Targets, Act Synergistically to Induce and Maintain Naive Pluripotency.

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Public Summary:

Activation of Wnt/beta-catenin signaling plays an important role in regulating embryonic stem cell (ESC) fate. To gain insights into the mechanism by which Wnt/beta-catenin regulates ESC fate, we screened and characterized genes induced by Wnt/beta-catenin signaling. Here, we show that the self-renewal-promoting effect of Wnt/beta-catenin signaling is mainly mediated by two of its downstream targets, Klf2 and Tfcp2l1. These two genes can promote reprogramming to and maintenance of ESCs. Our study therefore establishes the pivotal role of Klf2 and Tfcp2l1 in mediating ESC self-renewal promoted by Wnt/beta-catenin signaling.

Scientific Abstract:

Activation of Wnt/beta-catenin signaling can induce both self-renewal and differentiation in naive pluripotent embryonic stem cells (ESCs). To gain insights into the mechanism by which Wnt/beta-catenin regulates ESC fate, we screened and characterized its downstream targets. Here, we show that the self-renewal-promoting effect of Wnt/beta-catenin signaling is mainly mediated by two of its downstream targets, Klf2 and Tfcp2l1. Forced expression of Klf2 and Tfcp2l1 can not only induce reprogramming of primed state pluripotency into naive state ESCs, but also is sufficient to maintain the naive pluripotent state of ESCs. Conversely, downregulation of Klf2 and Tfcp2l1 impairs ESC self-renewal mediated by Wnt/beta-catenin signaling. Our study therefore establishes the pivotal role of Klf2 and Tfcp2l1 in mediating ESC self-renewal promoted by Wnt/beta-catenin signaling.

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